Message

From: onbehalfof+ehpmanuscripts+niehs.nih.gov@manuscriptcentral.com [onbehalfof+ehpmanuscripts+niehs.nih.gov@manuscriptcentral.com]
on behalf of ehpmanuscripts@niehs.nih.gov [ehpmanuscripts@niehs.nih.gov]
Sent: 2/12/2016 5:40:43 PM
To: Cogliano, Vincent [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=51f2736376ac4d32bad2fe7cfef2886b-Cogliano, Vincent]
Subject: Invitation to Review 15-10846-COM.R1 for EHP
Attachments: 15-10846-response.pdf

12-Feb-2016

Dear Dr. Cogliano:

Manuscript ID 15-10846-COM.R1 titled "AN INTEGRATED EXPERIMENTAL DESIGN FOR THE ASSESSMENT OF MULTIPLE TOXICOLOGICAL ENDPOINTS IN RAT BIOASSAYS" by Manservisi, Fabiana; Babot Marquillas, Clara; Buscaroli, Annalisa; Huff, James; Lauriola, Michelina; Mandrioli, Daniele; Manservigi, Marco; Panzacchi, Simona; Silbergeld, Ellen; Belpoggi, Fiorella has been submitted to Environmental Health Perspectives.

I invite you to review this REVISED manuscript (you reviewed the original submission). I have attached the authors' response to the original reviewer comments for your reference.

The abstract appears at the end of this letter. Please let me know as soon as possible if you will be able to accept my invitation to review. We prefer to receive review comments within two weeks of accepting the invitation, but if you need extra time please let us know and we can adjust the due date.

You may e-mail me with your reply or click the appropriate link at the bottom of the page to automatically register your reply with our online manuscript submission and review system.

Once you accept my invitation to review this manuscript, you will be notified via e-mail about how to access Manuscript Central, our online manuscript submission and review system. You will then have access to the manuscript and reviewer instructions in your Reviewer Center.

I realize that our expert reviewers greatly contribute to the high standards of the Journal, and I thank you for your present and/or future participation.

Sincerely,

Dr. Julian Preston
Environmental Health Perspectives
ehpmanuscripts@niehs.nih.gov

Agreed: https://mc.manuscriptcentral.com/ehp?URL_MASK=610c265370234ee396b51a5ef6008238

Declined: https://mc.manuscriptcentral.com/ehp?URL_MASK=b130dc1d927d4be290c14a0e126f2729

Unavailable: https://mc.manuscriptcentral.com/ehp?URL_MASK=48d665cd70224a5ab5ddfe024fa877a5

MANUSCRIPT DETAILS

TITLE: AN INTEGRATED EXPERIMENTAL DESIGN FOR THE ASSESSMENT OF MULTIPLE TOXICOLOGICAL ENDPOINTS IN RAT BIOASSAYS

ABSTRACT: BACKGROUND For nearly five decades long-term studies in rodents have been the accepted benchmark for assessing chronic long-term toxic effects, particularly carcinogenicity, of chemicals. The European Food Safety Authority (EFSA) and the World Health Organization (WHO) have pointed out that the current set of internationally utilized test methods capture only some of the potential adverse effects associated with exposures to these agents over the lifetime.

OBJECTIVES In this paper we propose the adaption of the carcinogenicity bioassay to integrate additional protocols for comprehensive long-term toxicity assessment that includes developmental exposures and long-term outcomes, capable of generating information on a broad spectrum of different endpoints.

DISCUSSION An integrated study design based on a stepwise process is described, that includes the priority endpoints of the OECD, NTP and EFSA guidelines on carcinogenicity/toxicity and developmental/reproductive toxicity. Integrating a comprehensive set of relevant toxicological endpoints in a single protocol represents an efficient opportunity, reducing animal use in accordance with the 3Rs (replacement, reduction and refinement). This strategy has the potential to provide sufficient data on

multiple windows of susceptibility of specific interest for risk assessments and public health decision making by including prenatal, lactational, neonatal exposures and evaluating outcomes over the lifespan. CONCLUSION This integrated study design is efficient in that the same generational cohort of rats used for evaluating long-term outcomes can be monitored in satellite parallel experiments to measure biomarkers and other parameters related to system-specific responses including metabolic alterations and endocrine disturbances.